

REMARKS

Applicants thank the Examiner for the indication of allowable subject matter and present new claim 114 - 123

Provisional Non-Statutory Double Patenting

Applicants acknowledge with appreciation the Examiner for the indication that the provisional Non-Statutory Double Patenting has been overcome.

Rejection under 35 U.S.C. § 112 ¶ 2

Claims 75-77, 87-89, 99-101 and 110-113 stand rejected under 112 second paragraph as being indefinite.

Claims 88, 95, 98, 107, and 110 have been cancelled, rendering their rejection moot.

Dependent claims 100 and 112 stand rejected as being indefinite. Claims 100 and 112 are limited to methods of treatment. The independent claims from which claims 100 and 112 depend, claims 90 and 102 respectively, encompass (but are not limited to) methods of treatment, as both are directed to “[a] method for treating or preventing retinal neovascularization in a mammal in need of treatment or prophylaxis.” These dependent claims narrow the independent claims, and do so in a clear way.

Claims 1, 78, 90 and 102 are allegedly indefinite for the recitation of “pterygium.” While Applicants neither agree with the Examiner, nor acquiesce to the Examiner’s position, in order to advance prosecution the term has been deleted from the claims.

Claims 77, 89, 101, and 113 are allegedly indefinite for failing to further limit the preceding claim and for the use of the term "implicate." While Applicants do not agree with the rejection or acquiesce to its correctness they have amended the claims to render the rejection moot.

The rejection of claim 110 is rendered moot by its cancellation.

Claims 75, 87, 99, and 111 are rejected as allegedly being indefinite for the recitation that of a batimastat compound and batimastat. While Applicants respectfully disagree with the Examiner, the Examiners suggested amendments to overcome this rejection have been adopted. Applicants respectfully submit the amendment does not alter the scope of the claims.

In view of the foregoing, Applicants submit that each rejection under 35 U.S.C. 112 second paragraph has been addressed or rendered moot; and Applicants request the rejections of record be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 78-86, 90-98, 102-110 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 5,767,153.

The Examiner rejects claims 78-86, 90-98, 102-110 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated on the grounds of inhency by U.S. Patent 5,767,153. In this respect the Examiner's attention is directed to the decisions in *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329 (Fed. Cir. 2003) and *Rapoport v. Dement*, 254 F.3d 1053 (Fed.Cir.2001). These cases make it clear where, as here, there is a recitation directed to a "method for treating (or preventing) retinal neovascularization in a mammal in need of such treatment (or

prophylaxis)” that recitation cannot be ignored. Indeed, in such instances the “claims are properly interpreted to mean ... [administration] to a human with a recognized need to treat or prevent” retinal neovascularization. *See Jansen*, 342 F.3d at 1334.

Furthermore, Applicants submit the Examiner has not set forth a *prima facie* case of anticipation. Applicants maintain the arguments set forth in the previous response, and note that the Examiner’s reliance on cases such as *Titanium Metals v. Banner*, which is directed to a product, as opposed to a process of using a product, is misplaced. Moreover, any assumption that a *prima facie* case of anticipation of can be made by asserting a process described by a reference can inherently set forth the intentional purpose for which the method must be performed is also incorrect.

The Examiner has acknowledged that the ’153 reference does not provide a disclosure of “... treatment of retinal neovascularization” by topical administration of the recited composition,¹ but the Examiner inappropriately relies upon inherency of disclosure to raise the inference that the missing limitation, the intentional purpose for which the method must be performed, necessarily flows from the ’153 disclosure in order to find anticipation under § 102(b). Applicants respectfully submit that the Examiner’s reliance on inherency of disclosure to meet the limitations of the claims is not, and cannot be, a teaching of “the intentional purpose for which the method must be performed,” and that a *prima facie* case of anticipation has not been presented.

¹ Office Action of October 8, 2004 at page 5; Office Action of May 6, 2005, at page 6, Office Action of December 21, 2005 at page 7.

For those reasons recited above, and the reasons of record, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102.

Rejection under 35 U.S.C. § 103

Claims 1-6, 71-74, 76-86, 88-98, 100, and 101 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US 5,767,153 in view of WO 97/41844.

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988), in which the prior art references applied must teach or suggest all of the claim limitations. *In re Royka*, 409 F.2d 981, 984 (CCPA 1974). In addition, there must be some suggestion or motivation to modify or combine references and there must be a reasonable expectation of success, *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). The suggestion, motivation to make the claimed combination, and the reasonable expectation of success, must be found in the prior art, and not based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d at 493.

The Examiner has taken the position that the phrase consisting essentially of can be construed as equivalent to comprising, and that based upon that position the previously pending claims are obvious in view of the combination of the '153 reference and the '844 reference. The Examiner alleges that "[s]ubstitution of polycarbophil suspension agent disclosed in US 5,767,153 for the generic suspension agent such as gel or the specifically exemplified tyloxapol suspension agent with the two angiostatic agents" would have been obvious. Applicants respectfully maintain that the '153 reference, alone or in combination with the '844 reference, cannot not render obvious the claims because the references do not teach all of the limitations of the claims, there exists neither a motivation to combine the references nor a reasonable expectation of success to derive Applicant's invention and the combination of the references as

suggested by the Examiner would render the invention described in the '844 reference inoperative.

Applicants respectfully disagree and submit that the analysis of their claims is based upon a false assumption. The term consisting essentially of cannot, in the present circumstances, be read as equivalent to comprising. The Examiner has acknowledged that the phrase "consisting essentially of" "limits the scope of a claim to the specified materials or steps and those that do not materially alter the basic and novel characteristics of the claimed invention." In addition, the Examiner asserts that Applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of Applicant's invention; while stating

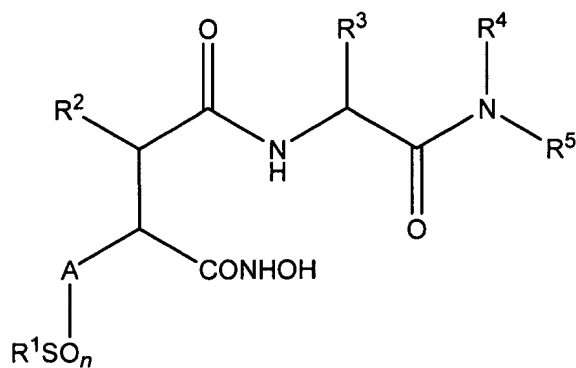
In the instant case, the characteristics of the composition used in the claimed method are still the same as the characteristics of the composition in the prior art reference of '844. That is the composition has MMP inhibitor activity, of which batimastat is one of the preferred MMP inhibitors and it can be topically applied to the eye to treat neovascularization.

Applicants respectfully submit that the basic and novel characteristics of the claimed invention cannot be the same as those of the '844 reference. The compositions set forth in the '844 reference require the use of two angiostatic agents, whereas the instant claims have only a single angiostatic agent. To ignore this is not only to ignore the fact that presence of two therapeutic agents is materially different than the presence of a single agent, but is also to ignore the underlying basis of the '844 disclosure, which is the use of a combination of angiostatic agents.

For at least the foregoing reasons, and those reasons set forth in subsections a-d, *infra*, Applicants respectfully submit that the rejections over US 5,767,153 in view of WO 97/41844 under 35 U.S.C. 103 should be withdrawn.

a. The '844 reference alone or in combination with the '153 reference does not teach all of the limitations of the claims

Applicants respectfully submit that the '844 reference, alone or in combination with the '153 reference cannot render obvious Applicants' claims. Whatever else the '844 reference teaches, it neither teaches nor fairly suggest methods for treating (or preventing) retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina, said composition comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent consisting essentially of a compound of formula I:



(I)...., as recited in independent claims 1 and 78.

Moreover, whatever else the '844 reference teaches, it neither teaches nor fairly suggest methods for treating (or preventing) retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a compound of formula I to the retina wherein said composition either "consisting essentially of a polymeric suspension agent, a compound of

formula I...,” or “consisting of a polymeric suspension agent, a compound of formula I...” as recited in independent claims 90 and 102.

Applicants further submit that the ‘153 reference cannot makeup for the deficiencies of the ‘844 reference, because as the Examiner has stated, “[t]he reference lacks disclosure of use of the composition of polycarbophil and batimastat for the treatment of retinal neovascularization.”

b. There is no motivation to combine the ‘153 and ‘844 references.

The Examiner contends that the cited art teaches the motivation to substitute the compositions of the ‘153 patent into methods of treating retinopathies allegedly taught in WO 97/41844 (the ‘844 reference). Applicants respectfully disagree. The claims are directed to methods “for treating (or preventing) retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina, the compositions “comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent *consisting essentially of* a compound of formula I...” a composition “consisting essentially of a polymeric suspension agent, a compound of formula I...,” or a composition “consisting of a polymeric suspension agent, a compound of formula I....” Whatever else the ‘844 reference teaches it neither teaches nor fairly suggests the use of such compositions, as it is directed to compositions comprised of two or more angiostatic agents. In this regard, the ‘844 reference states “[s]pecifically, the invention is directed to compositions containing two or more angiostatic agents. . . .”² In view of the foregoing, the ‘844 reference provides no motivation to combine the references and derive a method employing a single angiostatic agent as in the instant claims.

² See e.g., WO 97/41844 page 1, lines 13 – 15, and page 4, lines 21-22.

c. The '844 reference teaches away from its combination with the '153 reference.

To establish a *prima facie* case of obviousness, “some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” must be shown. *See, e.g., In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). No suggestion to combine references exists if a reference teaches away from its combination with another source. *See id* at 1075. “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant” *Tec Air Inc. v. Denso Mfg. Mich. Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999) (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed.Cir.1994)).

Applicants respectfully submit that the '844 reference teaches away from the instant invention because a person of ordinary skill would be led in a direction divergent from the path that was taken by the Applicants. As discussed above, the '844 reference teaches the use of “two or more” angiostatic agents in combination to treat neovascularization,³ because “current therapy for treatment of ocular neovascular disease is not very effective.”⁴ Since the '844 reference teaches using a combination of angiostatic agents because a current treatments are not very effective, a skilled artisan would not be led in the direction of using a composition “comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent consisting essentially of a compound of formula I,” a composition “consisting essentially of a polymeric suspension agent, a compound of formula I,” or a composition “consisting of a polymeric suspension agent, a compound of formula I.” Thus, the '844 reference teaches away from the instant invention. As a reference that teaches away from the claimed invention cannot

³ WO 97/41844 at page 4, line 24.

⁴ *Id.* at page 2, lines 13-14.

support a finding of obviousness in combination with another reference, Applicants respectfully submit that the claims as presently amended obviate any rejection under 35 U.S.C. § 103 over the '844 reference.

d. There is no reasonable expectation of success.

To establish a *prima facie* case of obviousness there must be a reasonable expectation of success. The Examiner asserted that a reasonable expectation of success in achieving treatment of retinal neovascularization with the recited compositions may be found in the references without specifically identifying where support for that expectation may be found.

Applicants respectfully submit that a reasonable expectation of success has *not* been established, and that the references *do not* support a reasonable expectation of success. More specifically, the '153 reference cannot support a reasonable expectation of success in treating retinal neovascularization as the Examiner has stated that the '153 reference does not provide a disclosure of "... treatment of retinal neovascularization." Furthermore, no reasonable expectation of success may be found in the '844 reference as the reference teaches the use of single angiostatic agents are not very effective⁵ as discussed in section c, above.

Claims 75, 87 and 99 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US 5,767,153 in view of WO 97/41844 and further in view of US 5,917,090.

Applicants respectfully submit that the '090 patent, which is cited for teaching compounds of formula I cannot cure the above mentioned deficiencies of US 5,767,153 in view of WO 97/41844, and therefore alone or in combination with the '153 and '844 reference cannot render obvious claims 75, 87, or 99.

⁵ Applicants maintain that this reference does not teach treatment of retinal neovascularization employing topically applied angiostatic agents.

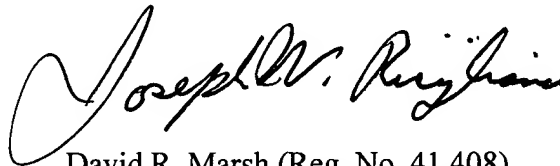
Applicants further note that the Office Action dated December 21, 2005 fails to substantively address claim 102 and its dependent claim, which employ the transitional phrase "consisting of" as opposed to consisting essentially of.

For the above reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing Applicants believe the application is in condition for allowance and they solicit a Notice of Allowance indicating such at the earliest possible time. The Examiner is encouraged to contact the undersigned should any additional information be necessary.

Respectfully submitted,



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**Admitted to practice in Virginia and before the U.S. Patent and Trademark Office only; practicing law in the District of Columbia pending approval of an application for admission to the D.C. Bar and under the supervision of attorneys who are members in good standing of the D.C. Bar.*

Date: March 21, 2006

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